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Ventilator-induced barotrauma in critically ill patients with COVID-19: a retrospective observational study

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ABSTRACT

Background: Ventilator-induced Barotrauma is a complication of intubation that is associated with high driving pressures and positive end-expiratory pressure use. We attempt to determine the incidence of barotrauma in intubated patients with SARS-CoV-2 infection.

Methods: Retrospective observation case series of patients with SARS-CoV-2 infection who were intubated in the ICU. Data were collected for a total of 3 months from electronic health records on patient's age, sex, BMI, incidence of barotrauma, total length of intubation and outcome.

Results: Ninteen out of the 100 included patients developed barotrauma as defined by radiographic evidence of pneumothorax, pneumomediastinum or subcutaneous emphysema. The average BMI of patients with barotrauma was 32.06 kg/m^2 with an average age of 56.84 years and 9 patients being classified as obese (BMI ≥30 kg/m^2). Fourteen out of 19 patients (73%) with barotrauma were intubated for 10 or more days with a median of 16.52 days. The overall mortality rate was noted to be 92% amongst intubated patients.

Conclusion: Rate of barotrauma in COVID-19 intubated patients was noted to be 19% in our study, which is on par with the rate of ventilator-induced barotrauma with the previous SARS virus-associated ARDS, and higher than that of the general population with ARDS. Patients who developed barotrauma were also noted to be intubated for a significantly longer duration (16.52 days) as compared to their non-barotrauma counterparts. These findings suggest a need for more data and randomized studies to establish appropriate ventilator management strategies for patients with lung injury associated with COVID-19.

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1. Introduction

Severe acute respiratory syndrome due to novel coronavirus (SARS-CoV-2) rapidly swept the entire world beginning in Wuhan, China in 2019–2020 and spread globally. The disease, now named COVID-19, primarily affects the pulmonary system and causes acute respiratory syndrome in severe cases often requiring supplemental oxygenation. Patients with significant disease require supplemental oxygen, often escalating to non-invasive mechanical ventilation and eventually deteriorating to invasive mechanical ventilation via endotracheal tube.

There is a plethora of literature that has established that higher positive end-expiratory pressure (PEEP) delivery via ventilation is a significant risk factor for incidence of barotrauma in patients with acute lung injury [1], as defined by the formation of pneumothorax, subcutaneous emphysema or pneumomediastinum. It is still unclear how intubation affects patients with severe acute respiratory syndrome due to COVID-19. Recently, with respect to COVID-19, it has been established that there is a higher risk of intubation and increased overall mortality risk in obese patients (as defined by BMI >30 kg/m^2), however this trend was primarily observed in patients younger than 65 years of age [2].

Due to the novelty and virulence of the virus resulting in progressive clinical deterioration, physicians and other medical personnel were unable to come to a consensus guideline for ventilation management in these patients. In order to obtain source control, the Center for Disease Control and Prevention (CDC) updated recommendations periodically regarding the management of COVID-19 patients and included avoidance of all aerosolizing procedures including nebulizers, inhalers, bronchoscopies, chest physiotherapy and non-invasive methods of mechanical ventilation unless considered emergent [3]. Furthermore, CDC also presented expert recommendations, which were then adopted by the American Academy of Head and Neck Surgery as well as other institutions who prohibited early tracheostomy placement, and to delay and reserve them for patients with stable pulmonary status [4,5].

The primary study objective was to examine the rate of barotrauma in ventilator-dependent COVID-19 patients. We also aim to define the patient characteristics

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in all intubated patients with COVID-19. In addition, we attempt to establish the overall risk of mortality in intubated patients with COVID-19 based on age and BMI sub-groups at our community hospital setting in the midst of the pandemic during its early phase in the United States. We also review and compare the previous literature regarding barotrauma risk associated with the previous SARS virus that swept the world in 2003. Furthermore, we examined and commented on the impact of guidelines put forth by the CDC regarding the management of patients with COVID-19.

2. Materials and methods

2.1. Study design

This retrospective study done in a Community Hospital ICU in New Jersey early in the pandemic beginning in April through June of 2020 included all patients positive for SARS-CoV-2 infection who were ventilator-dependent for respiratory failure and severe acute respiratory syndrome. IRB approval was obtained by the Chair of Institutional Review Board at the Hospital with study number TRMC2020-12. Informed Consent was not required as this was a retrospective observational analysis with no patient identifiers published. All participants' age, sex and BMI were all recorded at admission. Patients who were on non-invasive mechanical ventilation including CPAP or BiPAP at any time during their hospital stay were excluded. However, patients who received other forms of supplemental oxygen such as via Nasal Cannula, Non-Rebreather Mask and High-Flow therapy were included. The incidence of barotrauma was defined by the presence of subcutaneous emphysema, pneumothorax or pneumomediastinum in all intubated patients. Incidence of barotrauma was identified based on radiographic findings alone, either chest X-rays or CT scans. Total time in days on the ventilator was also documented, and end time was defined by either the day of tracheostomy tube placement, extubation or death.

Therefore, we established the incidence of barotrauma in ventilator-dependent respiratory failure in COVID-19 patients. We also reviewed patient characteristics including age, sex along with total days of intubation with the incidence of barotrauma. The overall incidence rate for barotrauma for intubated patients with SARS-CoV-2 infection was also determined and compared to data from previous studies in intubated patients with SARS infection from 2003 as noted in several articles found during our literature review.

In addition, mortality rate was calculated for all ventilator-dependent patients with COVID-19 during the study time period in the ICU, and stratified based on age and BMI groups as well.

2.2. Statistical analysis

The primary outcome measure was the incidence of barotrauma in ventilator-dependent COVID-19 patients in the ICU. Data were presented as an odds ratio and confidence interval. A p-value of less than 0.05 was considered to indicate the statistical significance and a 95% confidence interval was also utilized for validation of the data. In addition, the overall mortality rate was also calculated for all intubated patients with COVID-19, and then further stratified into age and BMI groups as well to establish further associations between the above-mentioned groups and mortality risk. Furthermore, we also analyzed the relationship between time spent intubated on a ventilator with the incidence of barotrauma, as well as the associated mortality risk.

Data regarding the overall incidence of barotrauma were compared to data found in our literature review concerning the incidence of barotrauma in ventilator-dependent patients with the SARS virus in 2003.

3. Results

Within the 3-month time period granted by the IRB for data collection, we analyzed a total of 100 patients intubated for COVID-19 in the ICU. Fifty of the included patients were noted to have a BMI ≥30 kg/m^2 and 50 with BMI <30 kg/m^2. The mean age for all intubated patients was 61.94 years with an average BMI of 31.53 kg/m^2. Among the intubated patients, 60 (60%) were male and 40 (40%) were female. A total of 92 out of the 100 patients enrolled in the study passed away either during ICU stay or on the general medical floors; amongst them, 56 (60.8%) were male and 36 were female (39.2%). The average age for patients with known mortality was 61.93 years with an average BMI of 31.74 kg/m^2. In addition, the average days on invasive mechanical ventilation for all patients were 10.15 days with average days on mechanical ventilation for patients who developed barotrauma being 16.52 days (Table 1).

Amongst the patients who developed barotrauma, males outnumbered females with an OR of 1.57 (95% CI 0.54–4.54). In addition, obese patients were found

Table 1. General characteristics of COVID-19 patients who developed barotrauma with intubation.

Age (years)	56.84	
BMI (kg/m^2)	32.06	
Sex	13 M (68.4%) 6 F (31.5%)	OR (Males) 1.57, 95% CI.54–4.54
Obesity	9/19 (47.36%)	OR = 0.87 95% CI 0.32–2.38
Length of intubation (days) >10 days (n)	16.52 14/19 (73.3%)	OR = 5.02, 95% CI 1.64–15.35 p = 0.004
Death (n)	19/19 (100%)	

to have an OR of 0.87 (95% CI 0.32–2.38). Nineteen patients from the 100 included patients in the study experienced barotrauma at some stage during their admission stay while intubated with an average BMI of 32.06 kg/m^2 and an average age of 56.84 years (Table 1). Thirteen (68.4%) patients who experienced barotrauma were male, and 6 (31.5%) were female. Nine out of 19 patients with barotrauma were noted to be obese (47.36%). Out of the original sample, Fifty-seven patients were intubated for less than 10 days, and Forty-three patients out of the original 100 patients were intubated 10 or more days; 14/43 (32.55%) of those patients developed barotrauma (OR = 5.02, 95% CI 1.64–15.35, $p = 0.004$) compared to 5/57 (8.77%) who were intubated less than 10 days. All 19 (100%) of the patients who did develop barotrauma passed away compared to 73 out of the 81 (90.1%) patients who died who did not develop barotrauma.

4. Discussion

Barotrauma as defined by pneumothorax (Figure 1), pneumomediastinum (Figure 2) or subcutaneous emphysema (Figure 3) is a known complication of invasive mechanical ventilation via intubation and has been established to occur secondary to increased PEEP and high driving pressures. In our study, 19% of patients with SARS-CoV-2 infection-related severe acute respiratory syndrome requiring mechanical ventilation developed ventilator-induced barotrauma. Further sub-group analysis revealed 14 patients (73.7%) with barotrauma were intubated for more than 10 days with an average length of intubation in barotrauma patients being 16.52 days. This was found to be significantly longer when compared to intubated patients who did not develop barotrauma who were intubated for a total of 8.63 days (Table 1). Unfortunately, all patients who developed barotrauma passed away while on the invasive mechanical ventilator.

As a result, it appears that length of intubation in patients with SARS-CoV-2 directly correlates with the risk of developing barotrauma. Although increased time on the ventilator itself can be a risk factor for barotrauma, it becomes worthwhile to note this trend as it may signify an increased risk of mortality in intubated patients with COVID-19 related severe acute respiratory syndrome. It is important to note, however, that since patients on non-invasive mechanical ventilation alone were excluded in our study, our results may not be generalizable to all measures of mechanical ventilation. In addition, due to the restrictions laid down by CDC, not all patients in our study who did develop barotrauma, especially pneumothoraxes, were able to have appropriate measures taken to resolve the complication. This could be considered a confounding variable as it could artificially inflate the mortality rate.

Since originating in Wuhan, SARS-CoV-2, a distant cousin of the original SARS virus that caused a pandemic in early 2003, has spread globally causing a pandemic. Upon review, there is limited literature regarding mechanically intubated patients with SARS virus (SARS-CoV) and association with barotrauma. In our retrospective study, 19% of patients developed barotrauma with mechanical intubation. In Lew et al. retrospective case series, 40 out of 199 patients with SARS-CoV developed severe acute respiratory syndrome requiring invasive mechanical intubation with 9 patients (22.5%) developing barotrauma [6]. Fowler et al. describe a case series with the SARS virus where 25 patients out of 196 patients required invasive mechanical ventilation and 10 out of the 25 patients (40%) developed barotrauma [7]. Kao et al. analyzed mechanically ventilated patients with SARS-CoV in a prospective case series and found out that 5 out of 41 intubated patients (12.2%) developed barotrauma [8].

As observable, the rates of barotrauma range from 12% to 40% with a mean of 24% in patients intubated with SARS-CoV, as compared to 19% from our retrospective case series in patients with SARS-CoV-2. Given that our study is the only one that analyzes the association between SARS-CoV-2 and incidence of barotrauma, it is difficult to corroborate and define a range for barotrauma in these patients. Furthermore, we included 100 patients that were intubated compared to a much lower number in each of the previously mentioned studies for SARS-CoV patients. However, it seems that the rate of barotrauma in patients who were intubated due to severe acute respiratory syndrome in SARS-CoV is higher than the rate of barotrauma in our study that focuses on patients with SARS-CoV-2. In addition, the general rate of ventilator-induced barotrauma with ARDS was found to be 13% [1], which appears to be lower than the rate of barotrauma in our study. There are several possible theories behind this finding; the most likely being that due to an increased degree of inflammation caused by both coronaviruses, there is a consequent need for increased oxygenation and PEEP requirements resulting in an increased rate of barotrauma. Another possible mechanism is direct parenchymal damage to alveoli altering pulmonary compliance caused by these viruses that would potentiate the risk of barotrauma in these patients as they are ventilated even at minimum PEEP requirements. The lack of an exact mechanism behind this finding again reflects the limited understanding we have regarding severe acute respiratory syndrome related to COVID-19 given its novelty.

As evident from our study, a 92% mortality rate in critically severe COVID-19 intubated patients is very high for any disease. Conjecture remains regarding

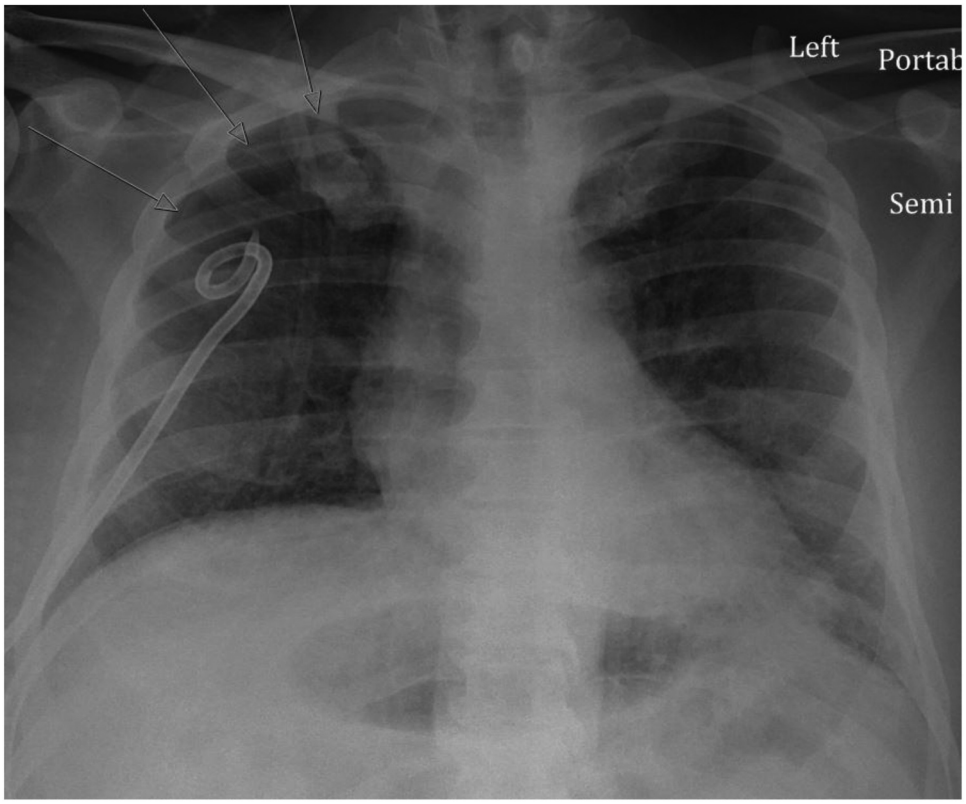

Figure 1. An Anterior-Posterior portable film demonstrating a small right-sided apical pneumothorax with fine bilateral reticular infiltrates within the lungs in an intubated patient with COVID-19.

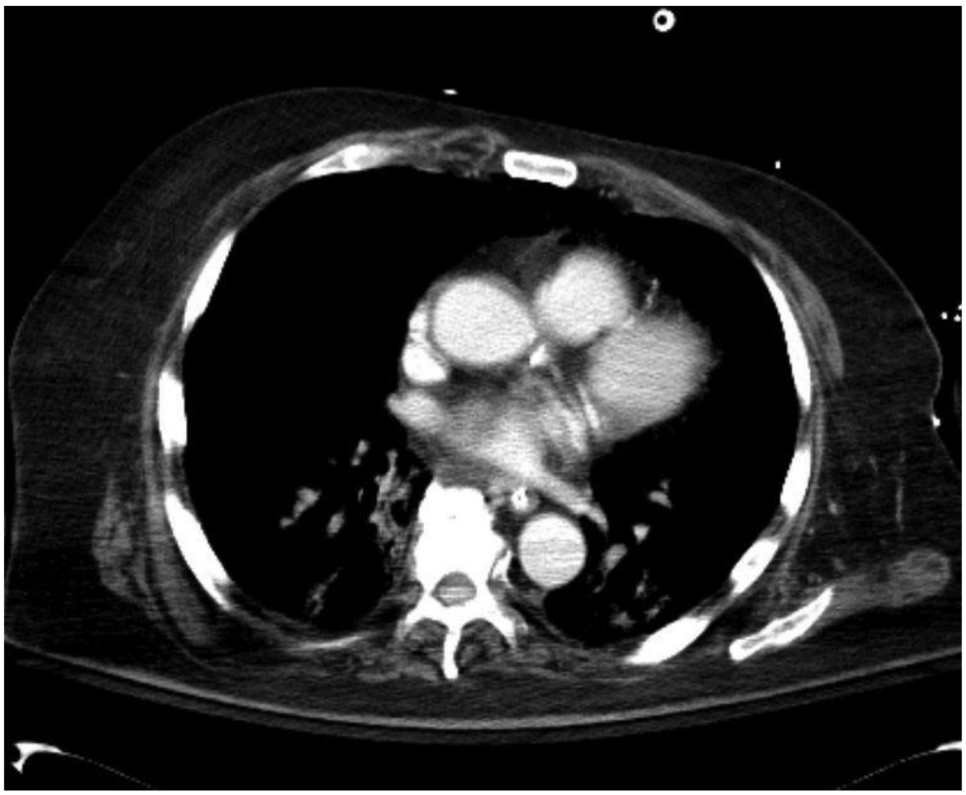

Figure 2. A CT abdomen with contrast demonstrating scant partial pneumomediastinum captured in an intubated patient with COVID-19.

the proper management with respect to ventilation and specifically the appropriate duration of continued mechanical ventilation via endotracheal tube and eventual transition to tracheostomy for these patients. In retrospect, as these patients were intubated for several days and never proceeded to tracheostomies

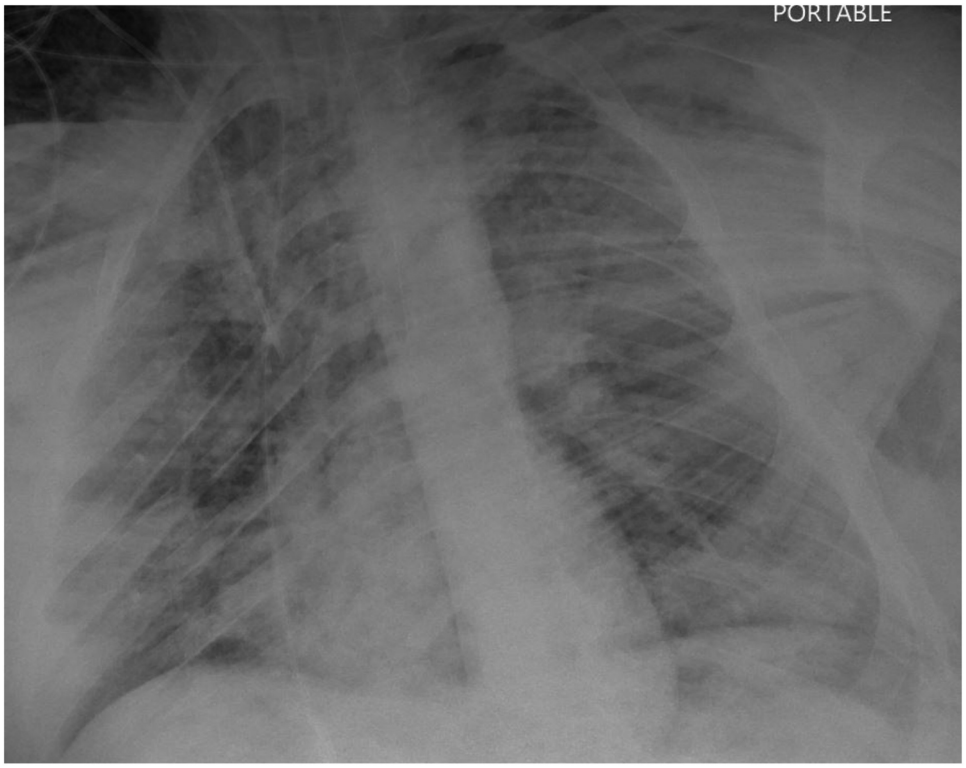

Figure 3. An Anterior-Posterior portable film demonstrating extensive soft-tissue subcutaneous emphysema with underlying patchy bilateral opacities within the lung in an intubated patient with COVID-19.

given restricted CDC guidelines mentioned earlier and hesitance of surgeons to perform the procedure, the 92% mortality rate may have been altered as a result. Additionally, as per CDC guidelines, treatments including the use of inhaled nebulizers with bronchodilators such as short-acting beta-agonists, bronchoscopies, and chest physiotherapy were all limited in these patients as it would possess a risk of aerosolizing virions and exposing them to medical staff [3–5]. Again, this illustrates another example of a potentially therapeutic management that was restricted from COVID-19 patients. This represents an ethical and moral dilemma as tracheostomy placements and medical therapies such as nebulizers, chest physiotherapy and bronchoscopies theoretically could have offered these patients symptomatic relief with an increased chance for survival and shorter time on and eventual weaning off the ventilator as well; On the contrary, the aforementioned interventions possess significant risks to physicians and other medical staff as it exposes them to aerosolizing droplets of the virus, which would further potentiate the spread and virulence of the virus. Therefore, physician and healthcare workers were crippled and handicapped when managing critical patients who were intubated due to COVID-19 as a lot of therapeutic interventions mentioned above posed a possible fatal risk for medical staff. As a result, in order to adequately define future recommendations and medical management strategies, there needs to be further discussion regarding the risks and benefits of allowing or restricting therapeutic strategies in COVID-19 while balancing the lives of both patients and medical personnel.

5. Limitations

There are several limitations in this study. First and foremost, as this a retrospective study instead of a randomized controlled trial, causality cannot be determined as to whether the incidence of ventilator-induced barotrauma in COVID-19 is higher than that of the general population in ARDS requiring mechanical ventilation. In addition, this study was performed in a single center ICU thereby limiting the generalization of the results.

Since the COVID-19 pandemic has progressed further, the current rate of barotrauma secondary to mechanical ventilation may be drastically different than the one determined in this study, which was performed early in the course of the pandemic. Furthermore, the development of medications such as Dexamethasone during the later stages of the current pandemic will confound the results if the study was performed today. Several other drugs including Remdesivir, High-titer convalescent plasma from COVID-19 patients are also available now, which are used early in the course of the disease to prevent progression to severe disease, which requires

mechanical ventilation as are the patients in our study [9,10].

6. Conclusion

The novelty of COVID-19 has led to several reports and case series that attempt to define the disease demographics and prognostic indicators. We define a 19% incidence of barotrauma in patients receiving invasive mechanical ventilation with critically severe COVID-19, which is congruent to the rate of barotrauma in SARS-CoV-2-related ARDS (12–40% in various studies). In addition, our study generated a higher rate of barotrauma as compared to the general incidence of barotrauma in intubated patients with ARDS as mentioned by Eisner, et al. [1] As we currently experience a resurgence in increased prevalence of COVID-19 cases in the United States, as physicians, we must weigh the risk of increased duration on mechanical ventilation in critically severe COVID-19 patients. Whether this is reflective of a need for early tracheostomies or an impetus for further research and studies to develop novel medical management strategies to avoid invasive mechanical ventilation. In addition, the spread of COVID-19 in the early spring of 2020 caused havoc and chaos in the Northeast region of the United States owing to its rapid spread compounded by delayed and inconsistent measures of source control. The dynamic and ever-changing CDC guidelines regarding appropriate oxygenation and ventilation management in these patients restricted several potentially therapeutic and quite possibly life-saving measures in patients with severe disease as defined by the onset of severe acute respiratory syndrome requiring intubation. These restrictions are one out of several possible explanations behind the extremely high mortality rate found in our study and generally across the New York City Area as well. However, in order to further concretely characterize these explanations, there is a need for more retrospective and prospective studies to be published in the literature that details the prognosis and possible therapeutic interventions in intubated patients with COVID-19.

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   a. Anuraag Sah: Primary Author, Principal Investigator, Conceived the ideas or experimental design of the study, Performed Data Collection & Analysis.
   b. Emilio J Fabian: Conceived the ideas or experimental design of the study, Performed Data Collection & Analysis, Provided revisions to scientific content of Manuscript, Provided grammatical revisions to Manuscript.
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